VOL. II, No. 7 July 1948

UNITED NATIONS

CHRONICLE OF THE WORLD HEALTH ORGANIZATION

International Control of Cholera, Smallpox and Plague
Control of Malaria
Insulin

WORLD HEALTH ORGANIZATION
INTERIM COMMISSION

350, Fifth Avenue
NEW YORK

Palais des Nations
GENEVA

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Note by the Editor. — The *WHO Chronicle* is published at the end of each month in English, French, Spanish, Russian and Chinese. The *Chronicle* is intended to summarize some of the activities of the Organization, without, however, claiming to be an authoritative record of the official views of the Interim Commission, which are set out in the *Official Records of the WHO*. All correspondence relating to it should be addressed to the Geneva Office. Those who may wish to reproduce the text of this publication or extracts therefrom, more especially in the medical Press, are entirely at liberty to do so.

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"... there is reason to hope that... it may be possible to put an end for ever to all exaggerated and extravagant quarantine measures which are still to be found in certain countries, and which wreck commerce and navigation, and yet fail to provide for public health any safeguards proportionate to the damage caused."

A. PROUST, 1896

The International Control of Cholera, Smallpox and Plague

A Note on the First Session of the Expert Committee on International Epidemic Control and the Three Joint OIHP-WHO Study Groups on the Pestilential Diseases

On 30 September 1848, the *Matteo Bruzzo* sailed from Genoa carrying two hundred passengers. Several cases of cholera were discovered on board during the voyage, and after unsuccessful attempts to enter a port, the ship was taken for quarantine purposes near the island of Pianosa in Italy. The passengers of the ship were finally permitted to land on 27 January 1849 at Leghorn (Livorno). Their journey from Genoa to Leghorn had lasted four months!

This and many similar incidents vividly demonstrate the problems which have confronted health authorities ever since quarantine regulations were adopted as defensive measures against the epidemics which repeatedly afflicted European populations.

There are only two ways of ensuring active defence against pestilential diseases: to eradicate the endemic foci or to maintain

a permanent control on everything coming out of, or passing through, the endemic or the temporarily contaminated areas.

The eradication alone of the endemic foci would relieve, once and for ever, large parts of the world from the constant danger of being stricken with cholera, smallpox or plague. But many years will elapse before this long-cherished dream of epidemiologists comes true. The suppression of the pestilential diseases is hardly imaginable without the existence throughout the world—including the remote endemic areas in Asia and Africa—of satisfactory sanitation, and without the complete suppression of such important vectors as are known to be transmitters of plague, yellow fever and exanthematic typhus. Until this is done, the public-health officer will have to rely largely on the quarantine measures which offer some security at the cost of much complication in international communications.

Are there any reasonable prospects of simplifying the international quarantine system without increasing the ever-present danger of new epidemic outbreaks ?

The Interim Commission examined this problem, and it was agreed that the mechanism of sanitary conventions now in force is no longer adequate. The present system was recognized to be too slow and unwieldy for effective control of the international spread of disease owing to the necessity of subjecting any new conventions to complex and protracted national legislative processes.[1] It was, therefore, proposed that the old conventions should be replaced by international health regulations, which should be formulated by the new organization. Once the regulations are adopted by the World Health Assembly, they " shall come into force for all Members after due notice has been given of their adoption . . . except for such Members as may notify the Director-General of rejection or reservations within the period of time stated in the notice ".[2]

An Expert Committee on International Epidemic Control was appointed " to examine the circumstances underlying the spread of the major epidemic diseases and to restate the principles which should serve as a basis for their international control. " [3]

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[1] It will be recalled that the convention signed on 17 January 1912 did not become effective until 17 October 1920.

[2] Article 22 of the WHO Constitution.

[3] In the terms of reference of the expert committee, *Off. Rec. WHO*, 6, 179.

The first session of the committee was preceded by the meeting in Paris of three study-groups which were set up jointly by the Office International d'Hygiène Publique and WHO to furnish expert advice on the pestilential diseases to the expert committee. The study-groups made observations on recently established facts which, in the opinion of their members, should be taken into consideration in the drafting of the new international sanitary regulations, and undertook or recommended investigation on points which still require elucidation. One study-group dealt with cholera and met from 5 to 7 April ; another considered smallpox and met from 8 to 10 April ; the third, which dealt with plague, typhus and some other diseases, met from 31 March to 3 April.

Cholera

If, generally speaking, the measures of defence against cholera can be said to have yielded satisfactory results, they do not appear to be entirely without fault. While large parts of the world are effectively protected, little has been done to attack the endemic foci which remain a permanent menace to the security of all. Another defect of the present system is that it inevitably results in abuses which sometimes interfere to an intolerable extent with the freedom of travelling of people coming from, or passing through, countries suspected of being cholera-infected. As was pointed out recently in one of the WHO periodicals, " the cool and competent advice of the experts who had drafted rules of protection against cholera embodied in the international sanitary conventions was set aside, and health administrations in a number of countries swayed by emotional pressure from an ill-informed public applied quarantine and other measures of self-protection at variance not only with their legal international obligations, but with modern medical science ".[4]

Better Quarantine

What is " medical examination " ? This question was often asked in relation to the quarantine measures against cholera, but the answer given was not always similar. The International Sanitary Convention, 1926, as amended by the International Sanitary Con-

[4] Biraud, Y. and Kaul, P. M. : *Epidem. Vital Statist. Rep.* (1948), 1, 141.

vention, 1944, provides that " the crew and passengers . . . of cholera-suspected ships . . . may be subjected to surveillance " (Article 31).

The term " surveillance " is defined to mean that " persons are not isolated but that . . . they may be subjected in the places of arrival to a medical examination ". But experience has shown that the term " medical examination ", as commonly used, was not sufficiently well defined, and it has remained a source of dispute. The study-group therefore suggested that " medical examination " as mentioned in the international sanitary conventions must be understood to include such laboratory examinations as are deemed necessary by health authorities (including rectal swabbing). This should be stated explicitly in the definitions to be given in the new international sanitary regulations now in course of preparation.

In view of the relative character of the immunity conferred by vaccination, it was thought that vaccinated persons should not be exempted from all measures of control by the international quarantine regulations.

Vaccination

Cholera vaccine was recognized to be of definite value in the prophylaxis of the disease, provided that it was prepared with vibrio strains of real antigenic potency. The immunity—which is known to be relative—is manifest as early as the fourth day after injection and reaches its full effectiveness on the eighth day, to last at least six months. A single injection of 1 ml. of vaccine confers an appreciable immunity and constitutes a proper procedure for mass-vaccination campaigns. Two injections at a week's interval are, however, preferable and should be given to individuals particularly exposed to contamination (sanitary, police, military and administrative personnel). There is no contra-indication to cholera vaccination, as it gives little or no reaction ; it can be applied to all ages provided care is taken in the case of infants to reduce the dose in proportion to body-weight.

Most of the vaccines now produced include at least two of the Ogawa, Inaba and Intermediate types of the vibrio. It will be recalled that the wisdom of utilizing a mixed vaccine has been questioned and that this problem was already studied by the Expert

Committee on Biological Standardization.[5] New substance for discussion was provided by the study-group, which confirmed that the Ogawa and Inaba types of cholera vibrio may be responsible for successive epidemics of equal severity in a particular area and that they do not have a fixed geographical distribution. These types do not appear to represent all true sub-species, as under laboratory conditions the Ogawa type may be transformed to the Inaba type, even though the reverse has not been observed.

An important point brought out by the discussions of the study-group, was that at the end of the disease and during convalescence an increasing proportion of the vibrios excreted by the patient are of the " rough " variety. Transformation from the " smooth " to the " rough " form corresponds to a loss of pathogenicity of the organism. No reversion from the " rough " to the " smooth " form has, so far, been observed. Some of these facts will have to be carefully weighed by the Expert Committee on Biological Standardization when a final decision is arrived at with regard to the definition of a universally acceptable anti-cholera vaccine.

Smallpox

The general discussion held by the study-group on the changes which may be necessary to secure effective defence against smallpox was preceded by a review of recent developments in knowledge regarding the pathogenic agent and its mode of transmission.

Pathogenic Agent

The mere demonstration of the presence of Paschen bodies could not be regarded, it was agreed, as a practical method of differential diagnosis. It was safer to rely on the characteristic fever which always precedes the eruption in smallpox and drops at the moment of its appearance, but which, in chickenpox, accompanies every bout of eruption. The research carried out by Burnet at the Walter and Eliza Hall Institute of Pathology and Medicine, Melbourne, on the agglutination of chicken cells with vaccine virus for the evaluation of antibodies and the degree of immunity was thought to be potentially valuable, and it was felt that the experiment should be repeated.

[5] *Chronicle WHO*, 2, 117.

More study appeared to be necessary on the agent responsible for the various clinical forms which the disease is known to assume. Available evidence seemed to confirm the identity of the virus in the mild and malignant forms, but the scientific data to this effect were not entirely convincing. It was therefore recommended that new studies be undertaken by means of cultures on egg media.

Contagion and Transmission

It has long been known that the transmission of smallpox commonly occurred during the various stages of the eruptive period, particularly those of vesiculation and decrustation, the virus being transmitted either by direct or by indirect contagion. The preventive measures at present in force are based on the assumption that this was the usual mechanism for transmission, but the opinion has been expressed that present knowledge on this matter does not exhaust all possibilities. The study-group, recognizing this, concentrated on the hypothesis—which was not yet proved, but which was recognized to be likely—that the enanthematous elements also helped to disseminate the virus through Pfluegge's droplets. It was recommended that the existence in bucco-pharyngeal secretions of the virus at the time of the enanthema and even during the various phases of the disease should be ascertained by means of cultures on chorio-allantoic membrane.

The duration of the incubation period has been variously described as ranging from eight to fifteen days. The study-group considered that the duration was usually twelve days and that the adoption for quarantine purposes of a fourteen-day period, as in previous conventions, would provide an adequate margin of security.

Vaccination

Vaccination still remains the outstanding measure of defence against the disease. The study-group recognized the superiority of calf lymph over vaccines grown *in vitro* or on chorio-allantoic membranes, it being recognized that in certain countries it is sometimes necessary to resort to passages in other animals to strengthen the activity of the virus. As regards the technique of vaccination, the " multiple pressure method " recommended by Leake [6] in 1927 was

[6] *Cf.* Memorandum on Vaccination against Smallpox, Memo. 312/MED. Ministry of Health, London, 1948.

preferred. As to the site, it was considered that, in infants, the arm remained the most satisfactory site. Hypodermic vaccination was considered a dangerous procedure.

Accidents which have occurred in vaccination from time to time, mostly in the form of grave or even fatal post-vaccinal encephalitis, have been used by a minority as a justification for hastily condemning smallpox vaccination. The study-group was firmly of the opinion that the danger of post-vaccinal encephalitis for a community is not to be compared with that of smallpox in the absence of vaccination. The best way to avoid this complication was to carry out primary vaccination well before school age. Newborn babies should be vaccinated between the third and sixth months. In the case of an epidemic, all children, irrespective of age, should be vaccinated. Finally, in view of the gravity of " generalized vaccinia " in infants suffering from eczema, such persons should be isolated from the other persons in their environment during the development of the vaccinal lesions.

The following definitions of reactions observed after re-vaccination were suggested for universal adoption.

Success : Characterized by a lesion identical to that of primary vaccination in its morphological characteristics as well as in terms of the duration of its development ; in other words, the lesion goes through the stages of macule, papule, vesicule, pustule and scab, and develops within the fourteen days after vaccination.

Accelerated reaction (i.e. *modified*, or *vaccinoid* reaction) : A vaccinal lesion which, after a maculo-papular stage, shows a vesicle between the third and eighth days and may end in the formation of a scab. The two characteristics by which such a lesion can be identified are : first, the formation of a vesicle, and, second, its development, which is definitely more rapid than in the case of a reaction to primary vaccination.

Precocious non-vesicular reaction (so called " immunity reaction ") : Characterized by the appearance, after the first day, of a vaccinal lesion which does not develop beyond the papulo-macular stage, is pruriginous, and disappears at the latest on the third day.

Various tests carried out show that this is not a reaction of susceptibility to animal proteins which serve as a base for this vaccine virus. It might be well to abandon the term " immunity reaction ",

since it is in reality the expression of an antigen-antibody reaction which does not necessarily imply that it is accompanied by immunity. This has been clearly demonstrated in cases of malignant smallpox in subjects re-vaccinated a short while before who displayed the so-called " immunity reaction ".

In conclusion, the study-group felt that the time was ripe for making a decided change in the present quarantine system against smallpox. Article 42 of the Conventions of 1926 and 1944 left it to the authorities of the country of arrival to decide whether or not the traveller had been adequately vaccinated. The study-group proposed, however, that all vaccination certificates which did not record a success or an accelerated reaction should be considered valid for six months only, while a doctor's statement, confirming that he had observed a reaction of either kind, should be valid for three years at least. Such a radical change may lead to satisfactory results, but implies also a fundamental change of principle.

The Expert Committee on International Epidemic Control, to which the question was referred, felt that the repercussions on national, as well as international, practice and legislation made it impossible to adopt the suggested change without further study. The final decision was, consequently, deferred to a later session.

Plague and Other Diseases

Although the time has not yet come for a general offensive against plague, the study-group was in a position to make a number of recommendations which, if applied, might result in a considerable relaxation of the present quarantine measures.

The use of insecticides with residual action such as DDT was recommended as the chief measure of international protection against plague.

Recently developed rodent poisons were found to produce efficient deratization. The combined use of insecticides and rodenticides would permit, in the opinion of the study-group, the eradication of plague from ports, towns and villages. It cannot, unfortunately, be of practical use in the fight against sylvatic enzootics.

It was agreed that disinsectization of merchandise coming from infected areas (as laid down under Article 17 of the 1926/44 Convention) should in some cases be supplemented by disinfection. In international air traffic, the proper use of insecticides on the air-

craft's departure from an infected area was found to provide adequate protection.

Although the incubation period for plague is not normally more than three days, it was recognized by the study-group that it could sometimes be longer and attain or even exceed the six-day period referred to in the conventions, especially in cases where infection is mild or alleviated by vaccination. However, it must be remembered that the length of the incubation period has lost a great deal of its importance from the international prophylactic point of view because of the efficiency of the new insecticides such as DDT.

The possibility was also considered that since infection of ecto-parasites takes place mostly during the last (septicæmic) stages of the disease, the marked curative action of sulfonamides and streptomycin may diminish the chances of secondary contamination.

*

Another problem discussed by the study-group was that of exanthematic typhus. It was agreed that the use of insecticides with residual action, such as DDT, should constitute, as in the case of plague, the essential measure of international protection against the disease and should permit the relaxation of other quarantine measures. In view of the danger of contamination by excreta of infected lice and fleas, disinfection as well as disinsectization of the effects of patients and contacts was recommended. For practical purposes, the incubation period of typhus was considered by the study-group to be of 14 days, and not of 12 days as previously stated in the international sanitary conventions.

A number of recommendations were also made by the study-group with regard to louse-borne relapsing fever, dengue fever, psittacosis, epidemic influenza, cerebrospinal meningitis, and poliomyelitis.

First Session of the Expert Committee on International Epidemic Control

The findings of the three study-groups[7] were transmitted to the Expert Committee on International Epidemic Control,[7] which met from 12 to 17 April 1948 in Geneva.

The committee agreed with the study-groups that protective measures taken by countries at their respective borders under

[7] For lists of participants, see *Chronicle WHO*, 1948 **2**, 104-105.

existing international sanitary conventions were only palliatives, as effective international control of epidemics required delimitation of endemic areas whence epidemics of the pestilential diseases originated. It recommended, therefore, a delimitation of the endemic zones as a first step towards an eventual attack on these endemic foci with the technical help of WHO, if needed. The committee also considered simplification and improvement of the present system of disseminating urgent information on pestilential diseases, and particularly the possibilities of extending the present system of broadcasting telegraphic epidemiological bulletins.

Finally, the committee decided to recommend the inclusion of louse-borne relapsing fever among the pestilential diseases, and to recommend the inclusion of cerebrospinal meningitis, dengue fever, epidemic influenza and poliomyelitis among the diseases for which immediate notification must be made in case of epidemic.

Control of Malaria

A Note on the Second Session of the Expert Committee on Malaria

Despite recent progress achieved in regard to malaria control, the incidence of the disease is still extremely high throughout a large portion of the globe. Millions of deaths and hundreds of millions of cases of malaria still occur annually. The reduced working capacity of populations physically and morally weakened by the disease has far-reaching economic consequences. From its essentially rural character, malaria is, perhaps, the scourge that most profoundly affects the agricultural worker, and hence the production of food, as was stated before the committee by representatives of FAO. In regions already under cultivation, malaria undermines the strength of the workers and diminishes the number of effective working days—often during the harvest, when all manpower should be available. On the other hand, malaria may prevent the development of regions where agriculture might have prospered. While the world is suffering from a shortage of food, and while the areas devoted to agriculture appear insufficient to meet all needs, the control of malaria in certain agricultural regions becomes an overriding necessity.

Methods recommended for the Eradication of Malaria

In the report on its first session [1] the committee briefly outlined modern methods of malaria control, but the second session was chiefly devoted to the part that WHO could play in assisting governments.

One of the most striking features of the report [2] of the second session held in Washington, 19-25 May 1948, is the evidence that it provides of the extent of the shift of emphasis from chemotherapeutic methods to mosquito control by the use of insecticides.

The following is an account of the committee's main conclusions :

Scope of Chemotherapy

Suppressive chemotherapy may be important as an emergency measure, especially during an epidemic, when the disease requires to be brought under control without delay. This should be done by treating the patients and by preventing the appearance of symptoms of the disease in subjects already infected by, or exposed to, anophelines. But thereafter, and as soon as possible, the vectors of the infection should be dealt with and a campaign against mosquitos should be organized.

Against endemic malaria, clinical prophylaxis (suppressive treatment) duly controlled, should be applied collectively when it is impossible to take steps for the eradication of mosquitos, as in the case of groups of workers, schoolchildren and armies in the field. Moreover, the fact that individual clinical prophylaxis still plays a considerable part should not be overlooked.

Choice of Drugs

Of the several available drugs :

Quinine remains valuable, especially in the case of serious infections with malignant tertian malaria ; it is not to be recommended for collective suppressive treatment, except in such countries as possess their own cinchona plantations.

Atabrine [3] is, without a doubt, an extremely efficacious suppressive, as experience during the second World War has shown. It

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[1] *Off. Rec. WHO*, **8**, 8 ; also extracts in *Bull. WHO*, 1947, **1**, 23-32 and notice in *Chronicle WHO*, 1947, **1**, 101.

[2] To be published in *Bull. WHO*, **1**, No. 2.

[3] *Synonyms :* Acriquine, Italchina, Mepacrine, Metoquina, Quinacrine.

is a sure means of preventing falciparum infection, but has disadvantages which do not apply to paludrine and chloroquine.

Chloroquine and *paludrine* produce the same results as atabrine, but are less toxic. The great advantage inherent in these two drugs is that they can be used for short courses of treatment, sometimes of a few days ; for suppressive purposes, one weekly dose is sufficient.

Treatment with chloroquine, which, according to trials in Venezuela, ensures radical cure of falciparum infections in only two days, would be most useful for outpatient treatment or self-medication ; the patient, who still feels ill after the first dose, is certain to take the second, whereas in the case of drugs which have to be taken over a longer period he may omit to continue the treatment once the symptoms have disappeared.

Paludrine is also suitable for self-medication, for a single dose can be sufficient to cure an attack—even if only clinically. This drug has exceptional advantages as a causal prophylactic against falciparum infections and also partly against vivax infections ; moreover, it has the property of arresting the cycle of development of the parasite in mosquitos, so that the latter can no longer spread the infection. Investigations of the dosage and action of paludrine on different strains of the parasite should, however, be pursued.

Relapses of vivax infection to-day constitute a problem that is all the more acute because falciparum infection, on the contrary, can be easily and completely cured by the use of the above-mentioned synthetic drugs. As yet, only two methods exist to deal with vivax infection: to continue suppressive treatment for a very long period, or to resort to combined treatment with a gametocide associated with a schizonticide—the old formula of plasmoquine combined with quinine, in which nowadays pentaquine or iso-pentaquine is substituted for plasmoquine. The latter two drugs, which are less toxic than plasmoquine, produce a very high percentage of radical cures ; and iso-pentaquine promises to be even more efficacious and less toxic than pentaquine. But both are as yet in an experimental stage.

Scope of Insecticides

Insecticides now make it possible to contemplate effective malaria control in most malarious countries. The residual method against adult mosquitos is the best evolved to date for large-scale control

in rural areas. In urban centres, the use of the same insecticides for larval control may prove less costly.

A very large number of insecticides has already been studied with a view to use in the eradication of anophelines. DDT is the best of all, and provides ideal conditions for the control of malaria because of its relatively low cost, its prolonged residual action, and its relatively low toxicity for men and domestic animals, not to mention the additional advantage arising from the destruction of house-haunting insects, other than mosquitos, which are liable to transmit infectious diseases.

The discovery of DDT-resistant strains of house-flies has given rise to some alarm. While no DDT-resistant anophelines have hitherto been encountered, the possibility must be reckoned with, and the effect of that insecticide upon mosquitos should be carefully watched. Doubts have been expressed concerning the efficacy of DDT against the most dangerous of malaria vectors, *Anopheles gambiae*, in Central Africa. It is, however, difficult to express definite views on the matter, since further experiments are necessary.

The committee recommended that an expert sub-committee on insecticides should be established to study all the questions still outstanding concerning the use of insecticides, and to establish international standards for insecticides and their formulations. This sub-committee could also stimulate the distribution of the spraying apparatus that would be most suitable for each region.

The economic balance between production and consumption of DDT throughout the world appears to be satisfactory. But, paradoxically enough, DDT is manufactured mostly in non-malarious countries, while those which are most in need of it do not produce it, and must import it; and the importer—in some cases, the Ministry of Health—is indeed often obliged to pay customs duty. It was recommended that all these questions should be referred to the appropriate bodies of the Economic and Social Council.

An International Policy of Control

There are three major technical obstacles to the worldwide use of new methods to control malaria : lack of organization of malaria-control services, insufficient knowledge of new techniques and, finally, lack of trained personnel.

Aid to Governments

Since the objective of WHO is to aid governments as effectively as possible in carrying out malaria control by the most modern methods, it will have to direct its efforts as follows :

(a) Assist governments, on request, to set up on a permanent basis control services suited to local needs and staffed by a suitably qualified and adequately paid staff. An essential condition for the effective control of malaria is that it shall be pursued at a cost which is the lowest feasible cost and proportionate to the budgetary capacity of the State concerned. To achieve this, WHO may have to furnish individual experts to advise governments creating such a service, or to improve existing services, and lend operational demonstration teams to begin the work. These teams should first carry out a survey of the selected area and then carry out a control programme by means of residual insecticides. The co-operation of such teams would be granted on condition that each member of the team was understudied by a local colleague, for it is understood that the programme of work of the teams shall thereafter be continued and developed by the host government.

The committee recommended that three of these teams be formed as early as possible, and that they should be allocated on request from governments to selected areas in Central Africa, South-East Asia and the tropical Americas. These regions would be selected after due consideration by the Secretariat of WHO in co-operation with that of FAO, on the basis of the feasibility of effective malaria control, and of its importance as regards increased food-production.

(b) Assist in existing schools of malariology, by sending foreign expert lecturers who would participate in the teaching programme and thus co-operate in the training of personnel: offer fellowships and travel grants for training in malariology ; consider the possibility of a revival of the international malariology courses formerly held at Singapore by the Health Organization of the League of Nations, and of organizing a similar course in Central Africa, where there is a particular need of trained personnel.

(c) Promote knowledge of modern methods of malaria control by the dissemination of reports and manuals, and by the circulation of material for the education of the public on this subject. When the regional organizations of WHO are established, it would be well for these to create a service for lending educative material for malaria. The committee finally observed that the training of government officials and of engineers of all branches is even more important than education of the public.

Research

In view of the gaps in present knowledge of certain aspects of chemotherapeutic drugs and insecticides, the committee recommended the following programme of research:

(a) Co-ordinated field and hospital trials in malaria therapy and prophylaxis in various countries; and

(b) An experiment in the eradication of the vector species in a selected Central African region, which must not be bounded or sheltered by natural barriers, but artificially protected against the re-introduction of the species by means of a campaign carried out at the periphery. The results of such an experiment would be of the highest importance in view of extension of anti-malaria campaigns in Africa.

Protection of Regions cleared of Anopheles

It is known that the eradication of the vector species is this year entering upon its final stages in two Mediterranean islands, Sardinia and Cyprus. With regard to the former, the committee shared the Italian Government's anxiety to avoid the re-importation of anophelines into the island once they have been eradicated. The Expert Committee on International Epidemic Control has sent the committee a draft international sanitary agreement and the committee has recommended to the World Health Assembly that measures similar to those provided for in the agreement be immediately enforced. It advised, however, that apart from the disinsectization of aircraft or ships, which may be left to the competence of the local authorities, an essential protective measure be taken — rigid anti-anopheline sanitation of ports and airports to ensure that no imported mosquitos survive.

The second session [4] of the committee followed the Fourth International Congresses on Tropical Medicine and Malaria, which were also held in Washington. Some seventy malariologists held an

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[4] *Expert Committee on Malaria:*

The following attended the session:

Major-General Sir Gordon COVELL, Ministry of Health Malaria Laboratory, Horton Hospital, Epsom, Surrey, United Kingdom.

Dr. A. GABALDÓN, Chief, Malaria Division, Ministry of Health and Social Welfare, Maracay, Venezuela, *(Chairman)*.

(Continued on following page)

ad hoc meeting during the Congresses.[5] This meeting was arranged with the assistance of the International Conference Division of the Department of State of the United States, and through the good offices of Dr. W. Sawyer, Secretary-General of the Congresses, as well as Dr. Mark F. Boyd, organizer of the malaria section.

Opinions were expressed, orally or in writing, concerning most questions on the agenda of the committee's second session. In drawing up its report, the committee has naturally taken note of the suggestions put forward. It considered itself fortunate in having thus been able to establish contact with the leading malaria-control experts from many parts of the world, and to have had the benefit of their extensive experience.

Dr. P. F. RUSSELL, International Health Division, Rockefeller Foundation, New York, United States of America.

Médecin Général Inspecteur M. A. VAUCEL, Directeur du Service de Santé colonial au Ministère de la France d'Outre-Mer, Paris, France.

Dr. D. K. VISWANATHAN, Assistant Director of Public Health, Poona, India.

Secretary: Dr. E. J. PAMPANA, member of the Secretariat of the Interim Commission.

Co-opted Members:

Lieutenant-Colonel M. K. AFRIDI, Director, Malaria Institute of Pakistan, Karachi, Pakistan.

Dr. J. W. FIELD, Acting Director, Institute for Medical Research, Kuala Lumpur, Malaya.

Dr. D. BAGSTER WILSON, Tanga, Tanganyika.

FAO Representative:

Dr. W. R. AYKROYD, Director, Nutrition Division, FAO, Washington, D.C., U.S.A.

Pan American Malaria Commission Observers:

Dr. C. A. ALVARADO, in charge of Malaria and Tropical Diseases, Tucuman, Argentina.

Dr. W. S. ANTUNES, Director, National Yellow Fever Services Department of National Health, Rio de Janeiro, Brazil.

Dr. L. VARGAS, Laboratory of Entomology, Institute of Public Health and Tropical Diseases, Mexico, D.F., Mexico.

Consultants:

Dr. G. R. COATNEY, Division of Tropical Diseases, National Institute of Health (U.S. Public Health Service), Bethesda, Md., U.S.A.

Dr. G. HUFF, Department of Bacteriology and Parasitology, University of Chicago, Ill., U.S.A.

Dr. L. SOPER, Director, Pan American Sanitary Bureau, Washington, D.C., U.S.A.

Dr. H. H. STAGE, Bureau of Entomology and Plant Quarantine, Department of Agriculture, Washington, D.C., U.S.A.

[5] See p. 157.

The present shortage of insulin—an important problem now engaging the attention of WHO [1]—is due not so much to a shortage of pancreas as to the failure to collect and treat all the glands obtained from slaughter-houses.

A discovery which may prove of great value in the conservation of pancreas glands has recently been made in Germany. In response to a request from WHO, Dr. Fr. Lindner, of the Biochemical Laboratory of Farbwerke Höchst, has kindly provided in the article below a description of the new method.

Preservation of Pancreas-glands without Refrigeration

At present, and possibly for many years to come, the pancreas glands of slaughtered animals and of fish are the only source of insulin. During and after the war, insulin producers have had great difficulty in recovering their raw material, mainly because of the absence of appropriate refrigeration installations.

Unless the glands are processed without delay, or refrigerated at low temperatures (—20° to —30°C.), their insulin content is rapidly lost. To find a means of preserving glands without refrigeration was therefore a problem of great importance.

After many unsuccessful experiments, a new process has been developed in the laboratories of the Farbwerke Höchst which answers these requirements.[2] This process is based on the principle of converting the pancreas-glands into a stable dry product by treating them with an anhydrous salt which binds their water content as water of crystallization. Anhydrous sodium sulphate is normally used for the purpose. As 142 grammes are required to bind 180 grammes of water, approximately 600 grammes of the salt are theoretically necessary to bind the water contained in 1 kilogramme of pancreas. In practice, however, 700 grammes are required. The dry preparation may be maintained at the degree of acidity required, for instance pH 5, by the addition of sodium hydrosulphate, tartaric acid, or any other suitable agent.

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[1] *Chronicle WHO*, 1948, 2, 55.

[2] Application for German Patent No. 75315 IV a/30 h filed on 21 June 1943.

The idea of *dehydrating* an organ in order to preserve it is not new.[3] But although the principle has already been applied by several workers to the preservation of pancreas [4], it has not so far yielded good results, mainly because these workers failed to recognize that it was essential that the glands should be disintegrated rapidly and thoroughly and treated with an anhydrous salt not after, but during, the disintegration. This process is most suitably performed in rapid cutting-machines of the type found in most butchers' shops (fig. 1).

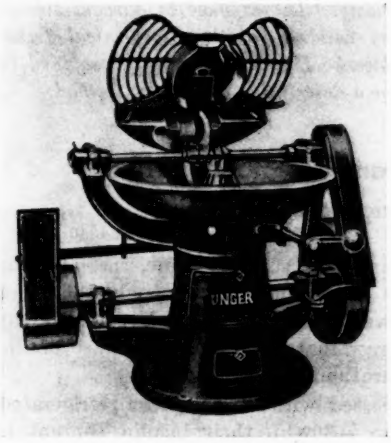

Fig. 1

The cutter consists of a rotating dish with a set of rapidly revolving sickle-shaped knives which simultaneously perform the disintegration and mixing, the pancreatic tissue being cut and its surface immediately brought into contact with the salt. One of the advantages of this new method is that since it is simple and safe, it can be applied without special training by the personnel of slaughter-houses.

In a large cutter, 12 to 15 kilogrammes of glands can be processed at a time, and, in the smaller cutters commonly found in butchers' shops, 8 to 10 kilogrammes. The glands should be collected and prepared as soon as possible after slaughtering, and then be kept in cold storage (5 - 8°C) until they are processed (not later than the same day). They are spread uniformly in the dish of the cutter and covered with 700 grammes of anhydrous, finely-ground sodium sulphate for each kilogramme of pancreas. The machine is then set in motion. After 8 to 10 minutes a homogeneous and rather compact mass is obtained and placed on iron sheets in a layer about 5 centimetres thick. The mass is then left for about one hour and taken into the refrigeration chamber for cold storage. By the next morning, the cakes will have solidified into slabs which are so hard and compact that they can be piled up without any special care.

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[3] See Fränkel, in Abderhalden, *Handbuch der biologischen Arbeitsmethoden*, Hamburg, 1936-1940, Sect. I, part 6, p. 4.

[4] See German Patent No. 441614 and British Patent No. 188660.

If the batches are too large and processing is delayed, difficulties are likely to arise, because the mass solidifies too rapidly.

The preparation obtained must be stored in as dry a place as possible at a temperature of 5-8°C (cold storage). Under these conditions, even after six months in storage, no loss of insulin occurs ; even storage at normal room-temperature—provided that it does not rise to 30°C—is tolerated for several days without damage, which greatly facilitates transport.

Insulin is obtained from this preparation in the usual way, with the same yield as is usually obtained from frozen glands.[5]

By applying the process described above, the Farbwerke Höchst were able to double the number of slaughter-houses from which they obtained the necessary pancreas glands for the production of insulin. It may be said that the new method has so far stood every test and has done much to stave off the worst consequences of the insulin shortage for diabetics in Germany.

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[5] Some difficulties in centrifuging were experienced at the beginning, owing to the salt content of the preparation.

NOTES FROM THE FIELD

Greece

Anæsthetics

The recent visit of the Unitarian Medical Services Mission from the U.S.A., which included amongst its members a Professor of Anæsthesiology, has stimulated the desire for progress in this subject. There is no specialist in anæsthetics in Greece at the present time, and open ether is generally the anæsthetists' choice. Certain surgeons have developed local anæsthetics to a considerable extent, but the absence of experience and equipment, together with the fact that nitrous oxide is not manufactured in Greece, has prevented the development of modern techniques. Negotiations were going on early in June between the Faculty of Medicine, Athens, the British Council, AMAG Public Health Division, and WHO as to the ways and means of providing an experienced anæsthetist from abroad who would go to Greece for a period of not less than twelve months and conduct a systematic course in this speciality.

Orthopædic Surgery and Rehabilitation

At the end of May, Dr. Henry Kessler, one of the most prominent American workers in orthopædic surgery and rehabilitation, visited Greece by invitation of the Minister of War.

On his arrival Dr. Kessler was engaged in lectures and demonstrations with some operative work, chiefly, though not entirely, in the military hospital in Athens. The WHO field mission was asked to make arrangements for him in Greece. A brief though extensive programme was devised in co-operation with the Ministry of Health, the Faculty of Medicine and another medical institution.

Public Health Nurses' Graduation

On 19 May, the first post-war group of sixteen public health nurses received their final graduation diplomas in the presence of Her Majesty Queen Fredericka. Most of these nurses will remain in Athens and work in the health centres and hospitals there.

Malaria Control

Reports have been recently received from the WHO field mission in Athens that 1,554 villages have been DDT residual sprayed up to 1 June.

NOTES AND NEWS

More about Insulin Production and Consumption

Two further replies, one from Argentina and one from Australia, have been received by the Secretariat in response to a questionnaire concerning insulin supplies which was sent to governments late in 1947. The production in these two countries roughly suffices to meet their needs; Australia, moreover, supplies New Zealand. The new data do not, therefore, modify the relationship between the quantities of insulin available and insulin requirements as given in a previous number of this journal.[1]

The position in these two countries is of great importance in view of their richness in raw material. Argentina exports 583 tons of frozen pancreas annually, which is processed in other countries. Australia, where about two million pigs are slaughtered annually, intends to resort to collecting pig pancreas. A thorough study of methods of extracting insulin may facilitate extraction from sheep pancreas, which is at present hampered by the high fat-content of that gland in the sheep. If this could be done, the twenty-two million sheep that are slaughtered yearly in Australia [2] could be turned to good account.

The search for new sources of insulin has revealed the possibility of using whale pancreas. In the blue whale, the pancreas is about 2.5 metres long, and weighs about 70 kilogrammes. The gland of the small whale weighs about 35 kilogrammes.[3]

During the period 1933-1940, some 43,000 whales were caught yearly; for the 1947-1948 whaling season the estimated catch is 25,000.

The extraction of insulin from cod pancreas, recently attempted in Germany, but abandoned by reason of its very high cost, appears to be of interest to certain firms engaged in cod-fishing and oil-extraction. These firms already possess the necessary technical equipment and may therefore be able eventually to reduce the cost and thus contribute to increase of supplies.

Informal Meeting on Malaria in Washington

An informal meeting, attended by 70 malariologists participating in the Fourth International Congresses on Tropical Medicine and Malaria, was held on 13 May in Washington, under the Chairmanship of Dr. A. Gabaldón. The object of the meeting was to afford an opportunity to participants to express their opinion upon a series of technical problems relating to the activities which WHO could carry out in the field of malaria.

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[1] *Chronicle WHO*, 1948, 2, 53.

[2] Statistics for the years 1938-1942.

[3] One kilogramme of whale pancreas may yield about 1,000 units of insulin.

According to Dr. L. W. Hackett, these activities should consist of exchanging technical information, of fostering research in general, of aiding research laboratories engaged in investigation of new insecticides, and of studying the collateral benefits to public health which result from the application of the residual-insecticide methods in malaria control.

The importance of interchanging experts, granting fellowships, and supplying technical literature, was emphasized by Dr. M. Pinotti, who at the same time pointed out the necessity of stimulating the study of the bionomics of malaria-carrying mosquitos in different parts of the world. Dr. H. P. S. Gilette, Dr. W. J. Stoker, and Dr. J. Clavero del Campo drew attention to the necessity for reducing the cost of DDT and of spraying equipment. The problem of Central African malaria was stressed by Dr. J. Schwetz. Professor G. Macdonald, supported by Dr. D. Bagster Wilson and Dr. L. J. Chwatt, emphasized the importance of attempting an experiment in anopheline eradication in a selected region in Central Africa. Such a region could be compared, in their opinion, to an artificial island, because having no natural barriers, it could be protected by a belt of residual insecticides. An experiment of such nature might shed much light on the question of the anti-malaria policy to be adopted in Africa.

The group heard an interesting and clear statement by Dr. C. A. Alvarado, who, on the basis of a large-scale campaign carried out in his country, showed that residual DDT puts the cost of malaria control below the level of the economic losses caused by the disease.

Several other speakers drew attention to the opportunity for WHO of re-establishing international malaria courses.

Visiting Lecturers in Poland and Finland

An international medical team, jointly sponsored by WHO and the American Unitarian Service Committee, is visiting a number of cities in Poland and Finland during July and August to describe and demonstrate some of the latest techniques in medicine and surgery. The team, headed by Dr. Leo Davidoff, Professor of Clinical Neurological Surgery at Columbia University College of Physicians and Surgeons, is composed of six American professors, who will be joined by British, Czechoslovak, Swedish and Swiss colleagues.

The work of this international group, the second of its kind to be organized by the Unitarian Service Committee under the sponsorship of WHO, [1] will be concentrated for six weeks in the universities of Warsaw, Krakow and Poznán, and in the Kosciuszko Hospital at Piekary, Poland. Following their activities in Poland, the group will proceed to Finland for a two weeks' stay at the universities of Helsinki and Turku.

A number of medical specialities will be represented. Particular emphasis will be placed on the various branches of surgery, such as neurological surgery, orthopædic surgery and chest surgery, in which notable advances

[1] For an account of the visit to Austria, see *Chronicle WHO*, 1947, 1, 113.

have been made in recent years. In addition, there will be specialists in general surgery, anæsthesiology, radiology and other subjects.

Other members of the mission are : Dr. W. Edward Chamberlain (radiology, Temple University, Philadelphia, Pa.), Dr. Joseph Charvat (medicine, Charles University, Prague), Dr. Robert Elman (clinical surgery, Washington University School of Medicine, St. Louis, Mo.), Dr. Eugene B. Ferris (medicine, University of Cincinnati, Ohio), Dr. Samuel Z. Levine (pædiatrics, Cornell University Medical College, New York). Dr. James E. M. Thomson (orthopædic surgery, Lincoln, Nebr.), Dr. S. Bernard Wortis (psychiatry, New York University College of Medicine, New York), Mr. C. Price Thomas (chest surgery, London), Dr. Robert Mackray (anæsthetics, London), Professor Jean Good (Basle), Professor C. Crafoord (chest surgery, Stockholm) and Dr. H. Good, (pulmonary thoracic surgery, Basle).

Reports from Poland show that the first phase has been an outstanding success. Particular mention is made of WHO's success in obtaining for the mission the services of no less than three teams of thoracic surgeons, at the urgent request of the Polish authorities. Mr. Price Thomas was operating at the Wolski Hospital in Warsaw during the first two weeks in July, and he has now been replaced by Professor Crafoord. Dr. H. Good begins a course on pulmonary thoracic surgery at Poznán on 27 July.

Fellowship Programme of the Interim Commission

The fellowship programme of the Interim Commission of WHO, which began in the early spring of 1947, ended during the interim phase of the organization this June.[1]

During its operation, fellowships were granted to doctors and other health personnel of twelve countries, these being placed in practically every European country, in the United States, and in Canada—countries in which the development of medical sciences and public health had continued during the war years, or which had recovered since the end of hostilities and were able to share their experiences with others.

Two hundred and seventy-four fellowships were granted for study in the medical sciences, clinical subjects, and public health. One hundred and fourteen fellows have now completed their studies and are already utilizing in their own countries their knowledge acquired during the study-tours. One hundred and sixty are still studying, or are awaiting transportation, and these will conclude their fellowships under the auspices of WHO itself.

During the course of the fellowship programme, a fellowship manual, based on actual experience, has been compiled, and effective working relations have been established with other organizations dealing with fellowships, aiming at the most satisfactory, and, as far as possible, uniform methods of administration.

Many new applications have been received by the New York and Geneva offices of WHO, the majority of them from fellows wishing to start in the

[1] For an account of the 1947 fellowship programme, see *Chronicle WHO*, 1948, 2, 3. The programme from its inception to mid-1948 is described in *Off. Rec. WHO*, 9, 5.

autumn of this year. The chief characteristic of these requests has been the growing number of candidates for fellowships in nursing, public-health nursing, occupational therapy, midwifery, sanitary engineering, and other branches of the large field of public health.

Resettlement of Specialists

From discussions at the General Conference on the Resettlement of Specialists (PCIRO), held in Gwatt, Switzerland, from 26 to 30 April 1948, which was attended by an observer of the Interim Commission, it appeared that the resettlement of nurses no longer presents any difficulties, the demand now being greater than the supply. As for doctors, although some progress has been made in the last six months, about 2,000 of them still await resettlement. Requests for small numbers of doctors have recently been received from Norway and Venezuela, but the greatest hope for rapid solution of the problem lies in the Bill now before the Congress of the United States of America, to admit into that country 200,000 displaced persons outside the quota, with doctors given the second highest priority.

A register of available doctors, with their qualification after screening, is being produced, and should be ready by July.

It was suggested that WHO should promote the standardization of the terminology of the various medical degrees issued by universities, and assess their value in different countries.

Maternal and Child Health

Following a decision taken by the Interim Commission at its fifth session to include the subject of maternal and child health as an item of the highest priority in the provisional agenda of the Health Assembly, Dr. Erkki A. Leppo, Deputy City Health Officer, Helsinki, was appointed to the Secretariat of the Interim Commission as expert on this subject.

WHO Representation

During the period between 1 June and 1 July, the Interim Commission was represented by observers who attended or took part in the meetings of the following organizations :

General Assembly, Second Session, ICAO, Geneva, 1 June.

Economic Commission for Latin America, Santiago, Chile, 7 June.

First International Congress on BCG, Paris-Lille, 18-23 June.

3.040 A., 2.040 F., 1.000 Esp., 8/48. Imprimerie de « La Tribune de Genève ».